APPENDIX A

"MARKED UP" CLAIMS ILLUSTRATING THE AMENDMENTS MADE TO THE CLAIMS OF 09/945,692 WITH ENTRY OF THIS AMENDMENT

Claims 277-274 have been canceled without prejudice to subsequent renewal.

New claims 278-296 have been added herein:

--278. (New) A method for evolving a polypeptide having an altered immunogenicity or stability, the polypeptide being encoded by a DNA substrate molecule, the method comprising:

(a) providing a library of variants of the DNA substrate molecule;

(b) transforming the variants of the DNA substrate molecule of (a) into host cells;

(c) expressing the variants of (b) to provide polypeptide expression products and derivatizing the polypeptide expression products with a moiety capable of altering immunogenicity or stability; and

(d) screening or selecting from the derivatized polypeptide expression products of (c) to identify at least one evolved polypeptide having an altered immunogenicity or stability relative to the polypeptide encoded by the DNA substrate molecule that is derivatized with the moiety.

279. (New) The method of claim 278, wherein the variants of (a) are generated by one or more of: recursive sequence recombination, PCR mutagenesis, cassette mutagenesis, oligonucleotide-directed mutagenesis, site-directed mutagenesis, doped oligo mutagenesis, chemical mutagenesis, or propagation of the DNA substrate molecule through bacterial mutator strains.

280. The method of claim 278, further comprising:

(e) recovering at least one evolved DNA substrate molecule encoding the at least one evolved polypeptide of (d); and

(f) subjecting the at least one evolved DNA substrate molecule of (e) to mutagenesis to generate mutagenized products.

281. (New) The method of claim 280, wherein the mutagenesis comprises one or more of: recursive sequence recombination, PCR mutagenesis, cassette mutagenesis,

oligonucleotide-directed mutagenesis, site-directed mutagenesis, doped oligo mutagenesis, chemical mutagenesis, or propagation of the DNA substrate molecule through bacterial mutator strains.

282. (New) The method of claim 278, wherein the moiety capable of altering immunogenicity or stability is a polymer.

283. (New) The method of claim 278, wherein the at least one evolved polypeptide has improved stability.

284. (New) The method of claim 278, wherein the at least one evolved polypeptide has reduced immunogenicity.

285. (New) The method of claim 278, wherein (c) comprises expressing the variants of (b) to provide polypeptide expression products, purifying the polypeptide expression products, and derivatizing the polypeptide expression products with a moiety capable of altering immunogenicity and/or stability.

286. (New) The method of claim 278, wherein the derivatized polypeptide expression products of (c) are derivatized post-translationally.

287. (New) The method of claim 278, wherein the at least one evolved polypeptide has reduced immunogenicity and improved stability.

288. (New) The method of claim 278, wherein the host cells comprise eukaryotic cells.

289. (New) The method of claim 280, wherein the mutagenized products are used as the library of variants in a repeated (a).

290. (New) A method for evolving a polypeptide having an altered immunogenicity, the polypeptide being encoded by a DNA substrate molecule, the method comprising:

(a) providing a library of variants of the DNA substrate molecule;

(b) transforming the variants of the DNA substrate molecule of (a) into host cells;

(c) expressing the variants of (b) to provide polypeptide expression products;

(d) screening or selecting from the polypeptide expression products of (c) to identify an evolved polypeptide having an altered immunogenicity relative to the polypeptide encoded by the DNA substrate molecule that is derivatized with the moiety;

(e) recovering an evolved DNA substrate molecule that encodes the evolved polypeptide of (d); and

(f) expressing the evolved DNA substrate molecule, thereby providing the evolved polypeptide having altered immunogenicity.

291. (New) The method of claim 290, wherein the altered immunogenicity comprises reduced immunogenicity.

292. (New) The method of claim 290, wherein the host cells comprise eukaryotic cells.

293. (New) A method of identifying a polypeptide having an altered immunogenicity or stability, the method comprising:

(a) providing a mixture of nucleic acid subsequences of two or more parental polynucleotides, wherein each parental polynucleotide differs from at least one other parental polynucleotide in at least one nucleotide and encodes at least one polypeptide or fragment thereof;

(b) extending one or more of the nucleic acid subsequences with at least one polymerase to produce one or more recombined polynucleotides that each encode one or more polypeptide variants;

(c) expressing the one or more recombined polynucleotides to provide the one or more polypeptide variants and derivatizing the one or more polypeptide variants with a moiety capable of altering immunogenicity or stability;

(d) screening or selecting the one or more polypeptide variants to identify at least one polypeptide variant having altered immunogenicity or stability compared to polypeptides derivatized with the moiety, which polypeptides are encoded by the two or more parental polynucleotides;

(e) recovering at least one recombined polynucleotide encoding the at least one cytokine variant identified in step (d); and

(f) repeating (a)-(d) using the at least one recombined polynucleotide recovered in step (e) as at least one of the two or more parental polynucleotides of a repeated step (a).

294. (New) The method of claim 293, wherein the host cells comprise eukaryotic cells.

295. (New) A method for evolving a polypeptide having an altered immunogenicity or stability, the polypeptide being encoded by a DNA substrate molecule, the method comprising:

(a) providing a library of variants of the DNA substrate molecule;

(b) transforming the variants of the DNA substrate molecule of (a) into host cells;

(c) expressing the variants of (b) to provide polypeptide expression products and derivatizing the polypeptide expression products with a moiety capable of altering immunogenicity or stability; and

(d) screening or selecting from the derivatized polypeptide expression products of (c) to identify at least one evolved polypeptide having an altered affinity for a receptor or a ligand relative to the polypeptide encoded by the DNA substrate molecule which polypeptide is derivatized with the moiety.

296. (New) The method of claim 295, wherein the host cells comprise eukaryotic cells.--